

REMARKS/ARGUMENTS

With this amendment, claims 6-34 are pending. Claims 1-5 and 35-55 are withdrawn. For convenience, the Examiner's rejections are addressed in the order presented in the September 5, 2006 Office Action.

I. Status of the claims

Claims 6 and 21 are amended to recite seeding the pancreatic cells isolated from a pancreas in a culture vessel, culturing the cells to induce expression of the CD56 protein, and then harvesting the pancreatic cells from the culture vessel. The cells are then contacted with a CD56 specific binding reagent. Support for this amendment is found throughout the specification, for example, at paragraph 140 on page 39, Example 6 on page 47, and paragraph 197 on page 47. This amendment adds no new matter.

II. Rejections under 35 U.S.C. 103(a)

Claims 6-34 are rejected as allegedly obvious over Fung *et al.*, (US Patent No. 6,326,201) and Shipley *et al.*, *Appl. Immunochem.* 5:87-93 (1997). The claims are directed to a method of obtaining a culture of propagating pancreatic cells that express a CD56 protein as a cell surface marker. Method steps include isolating pancreatic cells from a pancreas; contacting the pancreatic cells with a CD56 binding reagent; selecting pancreatic cells that specifically bind to the CD56 binding reagent; and separating the CD56 expressing cells from pancreatic cells that do not bind the CD56 binding reagent. To the extent the rejection applies to the amended claims, Applicants respectfully traverse the rejection.

The Office Action has not established a case of *prima facie* obviousness. To establish a *prima facie* case of obviousness, three basic criteria must be met: (1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) there must be a reasonable expectation of success; and (3) the prior art reference must teach or suggest all the claims limitations. MPEP§2143. See also *In re Rouffet*, 47

USPQ2d 1453. The court in *Rouffet* stated that "even when the level of skill in the art is high, the Board must identify specifically the principle, known to one of ordinary skill, that suggests the claimed combination." *Rouffet* at 1459. The court has also stated that actual evidence of a suggestion, or teaching, or motivation to combine is required and the showing of a suggestion, or teaching, or motivation to combine must be "clear and particular." *In re Dembiczak*, 50 USPQ2d 1614, 1617 (1999). The cited references do not meet this standard.

According to the Office Action Fung *et al.* teach a method of obtaining a culture of pancreatic cells using steps that allegedly include isolating cells using antibodies directed against specific proteins. The Office Action concedes that Fung *et al.* does not disclose using an anti-CD56 antibody. The Office Action alleges that Shipley *et al.* teach that CD56 is expressed on pancreatic islets and that this disclosure would lead one of skill to isolate pancreatic cells using the methods of Fung *et al.* Applicants provide a declaration from inventor, Dr. Wen-Ghii Tsang and other evidence to demonstrate that the teachings of Fung *et al.* and Shipley *et al.* do not provide a reasonable expectation of success in their combination and, moreover, cannot be combined to arrive at the claimed invention. The declaration and evidence are submitted as Exhibits A-E.

First, Shipley *et al.* disclosed expression of CD56 in islet cells, a type of differentiated pancreatic cell. Dr. Tsang states that the CD56 positive cells isolated using the claimed methods are dedifferentiated cells. Dr. Tsang also states, and provides evidence, that expression of a protein in a differentiated cell, such as an islet cell, does not predict that the same protein will be expressed in a less differentiated cell from the same tissue. Therefore, based on the disclosure of Shipley *et al.*, those of skill would not have a reasonable expectation of success in isolating undifferentiated pancreatic cells by selection with a CD56 binding reagent using the methods of Fung *et al.*

Second, Dr. Tsang provides evidence that the expression of CD56 in the claimed methods occurs after viable pancreatic cells are isolated and cultured. Dr. Tsang points out that an essential step of Shipley *et al.* is epitope retrieval of the CD56 protein to allow detection by the anti-CD-56 antibody. The essential retrieval step performed is application of microwave

radiation to the tissue. Dr. Tsang asserts that this microwave treatment would kill cells and thus, teaches away from culture of viable pancreatic cells to induce expression of the CD56 protein. Dr. Tsang also points out that Shipley *et al.* teach that their results are not consistent with FACS analysis using a CD56 antibody. Therefore, the methods of Fung *et al.* and Shipley *et al.* cannot be combined to arrive at the claimed invention.

Because the cited references do not provide a reasonable expectation of success in their combination and, in fact, cannot be combined to arrive at the claimed invention, the Office Action fails to provide a *prima facie* case of obviousness. Therefore, in view of the above arguments and remarks, withdrawal of the rejection for alleged obviousness is respectfully requested.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

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